large and small granules generated by his fractionation procedure. Claude described his first observations in the *Annual Report* for that year:

> The large particles from liver and mitochondria from leukemic cells under the electron microscope appear as perfect opaque spheres 0.5 to 1.6 μ in diameter. No definite membrane is evident in the prints. In instances where the granules are injured and some loss of substance has occurred, internal structure may be seen. Among these are small particles in the size range of microsomes. This observation taken with the fact that in the test tube disrupted large granules yield what appear to be microsomes suggests a relationship between these formations. (pp. 69–70)

He was not able to see any structure in the undamaged mitochondria because of their thickness, but if they had damage that allowed some material to escape, or were flattened somewhat during mounting, then the electron beam could penetrate them. Although Claude admitted in his published report (Claude & Fullam, 1945) that he could not see a membrane in the micrographs, he inferred its presence from the behavior of mitochondria in which some contents had escaped: "In some cases, loss of substance seems to release the tension which keeps the mitochondrial body spherical and, in such circumstances, the impression is gained that mitochondria possess a differentiated covering which may become more or less completely separated from the mitochondrial mass" (p. 57). Claude observed that mitochondria retained their shape and remained discrete if he used sufficient salt in the media employed in fractionation to insure proper tonicity. In opposition to Bensley's position, he contended that this disproved "the assumption that mitochondria may be formed by the concretion of substances preexisting in the cytoplasm or that they may disappear and reappear in living cells because of changes of equilibrium occurring in the surrounding protoplasm" (p. 58).

Claude's first use of the electron microscope provided little information about either mitochondria or the microsomes, but another approach would prove much more fruitful. The key person in this development was Keith Porter, who had joined the laboratory in 1939. Porter had completed his doctorate a year earlier at Harvard, pursuing research on the development of frog embryos with only a haploid set of chromosomes. This research required him to develop skills in micromanipulation of cells (e.g., removal of the nucleus before insemination so that the egg would develop with only the sperm's chromosomes). After he received his Ph.D., Porter was a postdoctoral fellow at Princeton, where he began to transplant the haploid nucleus of a frog of one geographically isolated race or subspecies into enucleated frog embryos of different races (Porter, 1941a; Porter, 1941b). Porter's ability to carry out these